REMARKS/ARGUMENTS

The present amendment constitutes a Request for Continued Examination under 37 C.F.R. § 1.114 in lieu of an appeal. Upon entry of this amendment, Claims 17-24 will be pending in the present application. Claims 1-16 were previously canceled, without prejudice. Claims 19 and 20 are amended herein. No new matter has been introduced by these amendments.

The specification has been amended with respect to the brief description of Fig. 6. The sequence listing has been amended at Item <213> of SEQ ID NOs:1 and 25 to remove the identifier "Homo sapiens". No new matter has been introduced by these amendments.

Applicant respectfully requests reconsideration of the rejections of record in view of the foregoing amendments and the following remarks.

Election/Restriction

The Examiner asserts that newly submitted Claim 17 (in part directed to fragments of at least 10 nucleotides) and Claims 21-24 are directed to an invention that is "independent or distinct" from the invention originally claimed. In particular, the Examiner asserts that "[t]he originally presented and elected invention was directed to Nit1 genes or nucleic acid encoding a Nit1 protein. Claim 17, in part, is directed to a fragment of at least 10 nucleotides of a DNA encoding a human Nit1 protein and claims 21-24 are directed to fragments of at least 10 nucleotides that are complementary to SEQ ID NO:1". (Office Action at page 2). The Examiner further asserts that receipt of a prior action on the merits of the original claims supports constructive election of only the original claims. On this basis, the Office Action states that Claim 17 (in part, as directed to fragments) and Claims 21-24 are withdrawn from consideration. Applicant respectfully requests reconsideration of the subject Restriction Requirement and constructive election.

The present response includes a Request for Continued Examination, which is believed to obviate the constructive election and avails Applicant of an opportunity to request reconsideration of the Restriction Requirement. Applicant respectfully submits that the subject matter relating to fragments of at least 10 nucleotides of Nit1 does not present an undue burden on the office with respect to searching and examining the application. On the

contrary, such subject matter should already be within the scope of subject matter searched for the comprehensive genus originally presented directed to Nit1 sequences. For the foregoing reasons, reconsideration and withdrawal of the Restriction Requirement, and examination of all pending claims on the merits, is earnestly solicited.

The Description of Figure 6 Does Not Contain New Matter

The amendment filed 11/5/02 has been objected to under 35 U.S.C. §132 as containing new matter with respect to the description of Figure 6. As amended herein, the description of Fig. 6 is correct and does not contain new matter. The original brief description clearly indicated that Fig. 6 referred to a sequence of a *NIT1* gene. (*See* as-filed specification at page 6, lines 4-5). Applicant notes with appreciation that the Examiner states that Fig. 6 by "comparison to original Fig. 1 appears to be a human sequence" due to its similarity to the human NIT1 amino acid sequence disclosed in Fig. 1. Furthermore, "[c]omparison to the other sequences of Fig. 1 clearly shows that the . . . sequence of Fig. 6 is not a murine, *D. melanogaster*, or *C. elegans* sequence." (Office Action at page 4). Therefore, one of ordinary skill in the art would have concluded, based upon the original disclosure, that Figure 6 represented human NIT1 sequences. Nonetheless, to advance the prosecution of the present application, the brief description of Fig. 6 as amended herein no longer refers to the depicted sequences as being human in origin.

The Examiner also objects to the previously-amended description of Figure 6, which refers to a splice variant of Nit1, as allegedly containing new matter. Without conceding the correctness of this objection, and to advance the prosecution of the present application, Applicant has herein amended the brief description of Fig. 6 such that it no longer refers to a splice variant. The objection has been obviated, and applicant respectfully requests withdrawal thereof.

Sequence Listing

The Amendment filed on 3/4/02 has been objected to under 35 U.S.C. §132 as allegedly introducing new matter. Specifically, the Examiner asserts that the sequence listing contains new matter at Item <213> of SEQ ID NOs: 1 and 25 because these sequences are

identified as being human in origin. As discussed *supra*, Applicant respectfully traverses this rejection. However, in the interest of advancing the prosecution of the present application, the sequence listing has been amended at Item <213> of SEQ ID NOs: 1 and 25 to read "cDNA Sequence" and "Polypeptide Sequence", respectively. A paper copy and computer readable form of the substitute sequence listing are provided herewith. The information recorded in the computer readable form is identical to that in the paper copy. A Statement to Support the Filing and Submission of the Sequence Listing also is submitted herewith. No new matter has been introduced. Applicant respectfully requests entry of the Substitute Sequence Listing.

The utility requirement of 35 U.S.C. §101 and the enablement requirement of 35 U.S.C. §112, first paragraph are met

Claims 18-20 stand rejected under 35 U.S.C. §101 and 35 U.S.C. §112, first paragraph, on the ground that the invention as claimed (1) lacks a specific and substantial asserted utility and lacks a well-established utility, and therefore (2) one of skill in the art would not be enabled to practice the claimed invention. Applicant respectfully traverses both rejections.

A strong relationship between Nit and Fhit has been established. As disclosed in the present specification at page 15, lines 11-27, there are well-established examples of eukaryotic biosynthetic pathways in which multiple steps are catalyzed by multifunctional proteins containing two or more enzymatic domains. The same steps in prokaryotes frequently are carried out by monoenzymatic proteins that are homologs of each domain of the corresponding eukaryotic protein. In such examples, if domains of a multienzymatic protein in some organisms are expressed as individual proteins in other organisms, the individual proteins participate in the same pathways. As the Examiner has noted, the present specification discloses that the expression of Nit in mice is almost identical to the pattern of expression of Fhit. (*See* Office Action at page 6, specification at page 15, lines 24-27). This indicates conservation of the relationship between Nit and Fhit throughout evolution, including mammals.

It is well documented that Fhit is associated with human disease, specifically cancer. Attached hereto are a number of references demonstrating the relationship between Fhit and human cancer. Ohta M, et al. *Cell* 1996; 84: 587-597, refers to data indicating that the human FHIT gene is abnormal in digestive tract cancers. Sozzi G, et al., *Cell* 1996; 85:17-26, refers to data indicating that the FHIT gene is abnormal in human lung cancer. Sozzi G, et al., *Cancer Res* 1998; 58:5032-5037 refers to data indicating that loss of FHIT function occurs in a very high percentage of human primary lung carcinomas and precancerous bronchial lesions. Siprashvili Z, et al., *Proc Natl Acad Sci USA* 1997; 94:13771-13776 refers to data indicating that replacement of Fhit suppresses tumorigenicity in a number of types of cancer cells that normally do not express Fhit.

As demonstrated by the attached references, one of skill in the art would have been aware of the well-established connection between Fhit and a number of human cancers. This, taken together with the relationship between Nit and Fhit that is well-conserved throughout evolution from *C. elegans* to humans (*see, e.g.*, present specification at page 15, lines 6-10; Fig. 1), provides support that Nit expression correlates with cancer in humans. Thus, the utility of Nit sequences for diagnosing and/or screening for human cancer is well-established.

The present specification also asserts specific, substantial and credible utilities for the claimed sequences. For instance, the specification states that the claimed sequences can be used as diagnostic and therapeutic reagents for the detection and treatment of *cancer* (page 1, lines 21-25). Thus, a specific utility has been asserted. Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as lacking credibility. (*See* United States Patent and Trademark Office (USPTO "Utility Examination Guidelines"). A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept the asserted utility. As noted in the Guidelines, "nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned". Furthermore, the asserted use with respect to a specific disease, cancer, is a utility that defines a "real world" use and thus represents a substantial utility.

Thus, the claimed invention is supported by both well-established utilities and asserted utilities that are specific, substantial and credible, thereby meeting the utility requirement of 35 U.S.C. §101. That being the case, one of skill in the art would be enabled

to use the invention, such that the enablement requirement of 35 U.S.C. §112, first paragraph is also satisfied. Accordingly, withdrawal of both rejections is respectfully requested.

An information disclosure statement (IDS) citing, *inter alia*, the documents discussed above, is being filed concurrently with the present response. The Examiner is respectfully requested to consider and initial the cited references.

Claims 19 and 20 Are Supported by Adequate Written Description

Claims 19 and 20 have been rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to meet the written description requirement, based upon dependency on Claim 17, which specifies human NIT1 sequences. As discussed *supra*, the Examiner has alleged that certain NIT1 sequences described in the present application were not adequately described. While Applicant respectfully traverses this rejection and asserts that the specification as filed did adequately disclose that SEQ ID NO:1 encodes a human NIT1 sequence, see discussion *supra*, for purposes of advancing the prosecution of this application Claims 19 and 20 have been amended such that they no longer depend from Claim 17.

Accordingly, Applicant asserts that the claims meet the written description requirement of 35 U.S.C. §112, first paragraph. Withdrawal of this rejection is respectfully requested.

Conclusion

In view of the foregoing, Applicant believes that, upon entry of this amendment, all claims now pending in this application are in condition for allowance. An early notification to that effect is respectfully requested.

References Cited

Ohta M, et al., *Cell* 1996; 84: 587-597.

Sozzi G, et al., *Cell* 1996; 85:17-26.

Sozzi G, et al., *Cancer Res* 1998; 58:5032-5037.

Siprashvili Z, et al., *Proc Natl Acad Sci USA* 1997; 94:13771-13776.

Respectfully submitted,

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